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Is vitamin D testing at a tertiary referral hospital consistent with guideline recommendations?

KATHERINE NORTON[1], SAMUEL D. VASIKARAN[1], GERARD T. CHEW[1,2,3] AND PAUL GLENDENNING[1,2]

[1]Department of Clinical Biochemistry, Royal Perth Hospital, [2]School of Medicine and Pharmacology, University of Western Australia, and [3]Department of Endocrinology and Diabetes, Royal Perth Hospital, Perth, WA, Australia

Summary

To determine if 25 hydroxyvitamin D (25OHD) testing at our tertiary referral hospital is consistent with guideline recommendations concerning the clinical indications for testing, the timing of repeat testing and utilisation of the test result, we conducted a retrospective audit of electronic laboratory and patient case records. We included adult inpatients and outpatients who had serum 25OHD measured during a randomly selected one-week audit period and who had patient case records available for detailed review. The audit sample comprised 184 serum 25OHD measurements (134 initial and 50 repeat tests). There were 81 (60%) initial and 15 (30%) repeat tests [96 (52%) overall] that were consistent with guideline recommendations concerning clinical indication, timing of repeat testing and utilisation of result. Almost half the 25 hydroxyvitamin D tests audited were potentially unnecessary and/or not utilised clinically. Improved adherence to guideline recommendations for 25 hydroxyvitamin D testing, utilisation of test results and enforcement of new indications for testing due to be introduced by Medicare Australia could result in significant cost savings without adversely affecting patient outcomes.

Key words: Guideline recommendations, test ordering, vitamin D.

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INTRODUCTION

Vitamin D testing in Australia has increased manifold in recent years, a trend echoed internationally, raising concerns that this could reflect excessive and inappropriate 'over-testing'.[1,2] However, interpretation of these data is limited because they were based only on test request numbers, without evaluation of the reason for initial and repeat testing, or whether testing affected clinical management.

Vitamin D deficiency (VDD) is causally linked with osteomalacia and rickets, falls, osteoporosis and fracture risk, and randomised clinical trial data demonstrate that vitamin D supplementation (with calcium) reduces falls and fractures in high risk populations.[3] Many observational studies have also shown VDD to be associated with a diverse range of illnesses but interpretation of these data may be limited by potential residual confounding, reverse causation and other biases. Low serum 25-hydroxyvitamin D (25OHD) could, in fact, be a marker, rather than cause, of ill health, as suggested by interventional trial data that do not support the efficacy of vitamin D supplementation in reducing the occurrence or severity of these extra-skeletal disorders.[4,5] The increase in test numbers is not surprising, perhaps, given the enormous number of publications related to VDD in recent years (more than 4000 in 2013 alone) and the large number of existing guidelines on the topic, which give seemingly disparate statements. Nevertheless, continued interest in the potential role of VDD as a possible risk factor for a wide variety of diseases may provide clinicians some leeway to adopt general principles rather than specific guideline recommendations when measuring serum 25OHD, leading to 'leakage' of the clinical indications for testing and increased testing.

The objective of this audit was to evaluate whether 25OHD testing at our tertiary referral hospital was consistent with published guideline recommendations concerning clinical indications for testing, timing of repeat testing and utilisation of the test result.

MATERIALS AND METHODS

We reviewed the major national and international guidelines relating to VDD and 25OHD testing published since 2010. The guidelines most relevant to local practice were assumed to be the conjoint Australia and New Zealand Bone and Mineral Society, Endocrine Society of Australia and Osteoporosis Australia position statement, published in 2012 which defines VDD as serum 25OHD <50 nmol/L at the end of winter and advocates retesting no earlier than 90 days after the initiation of vitamin D supplementation.[6] The Royal College of Pathologists of Australasia's (RCPA) position statement on the use and interpretation of vitamin D testing was subsequently published the year following the audit period and uses the same definition for VDD and recommendation for retesting.[7] Importantly, the clinical indications for testing in the RCPA position statement have been adopted by Medicare Australia to impose restrictions on 25OHD testing from 1 November 2014.

There are also three recently published major international guidelines relating to VDD and the management of osteoporosis, the key points of which are presented in Table 1 for comparison with the Australian guidelines.[8–10] Although the definitions of at-risk populations vary between guidelines, they generally include patients with conditions that have a known physiological mechanism for reduced synthesis or increased catabolism of vitamin D but not conditions without direct evidence of a causal link to VDD or benefit from vitamin D supplementation.

We collectively reviewed the existing guidelines and made a consensus *a priori* decision regarding the risk factors and medical conditions we would consider as 'guideline-supported' indications for 25OHD testing. These encompassed the majority of the indications listed in the various guidelines, including osteoporosis, falls, fracture, institutional residence, at-risk ethnicity (taken as Aboriginal or non-Caucasian descent, if skin tone not recorded), conditions associated with gastrointestinal malabsorption (Crohn's disease, short gut syndrome, bariatric surgery, chronic diarrhoea, cystic fibrosis, coeliac disease), chronic kidney disease (Stage 3–5 CKD or nephrotic range proteinuria), hepatic failure, infection (limited to latent tuberculosis or human immunodeficiency virus) and pharmacological therapy with glucocorticoids, azole antifungals,

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Table 1 Comparison of the Australian and international guidelines regarding vitamin D deficiency and testing (2010–2013)

	Australia and New Zealand Bone and Mineral Society, Endocrine Society of Australia and Osteoporosis Australia 2012[6]	Royal College of Pathologists of Australasia 2013[7]	International Osteoporosis Foundation 2010[8]	Endocrine Society (US) 2011[9]	European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis 2013[10]
Terminology	Adequacy: ≥50 nmol/L (end of winter) Deficiency: Mild: 30–49 nmol/L Moderate: 12.5–29 nmol/L Severe: <12.5 nmol/L	Decision limit: 50 nmol/L	Target level: 75 nmol/L Insufficiency: <50 or <75 nmol/L Deficiency: <25 nmol/L	Sufficiency: 75–250 nmol/L Insufficiency: 52.5–72.5 nmol/L Deficiency: <50 nmol/L	Sufficiency: 50–125 nmol/L Insufficiency: 25–49 nmol/L Deficiency: <25 nmol/L
Goal of therapy	≥50 nmol/L (end of winter)	>50 nmol/L (end of winter)	>75 nmol/L	>75 nmol/L	>50 nmol/L >75 nmol/L (fragile elderly at increased risk of falls and fractures)
At risk groups to be tested	Older age or disability, housebound or in residential care; dark skin, limited sun exposure; obesity	Osteomalacia, osteoporosis; isolated raised alkaline phosphatase; hyperparathyroidism, hyper- or hypocalcaemia, hypophosphataemia; malabsorption; dark skin, limited sun exposure; medications affecting vitamin D*; chronic kidney disease, renal transplant	Osteoporosis; malabsorption; limited sun exposure; institutionalised or housebound; non-European high-risk ethnicity (Middle Eastern, South Asian); obesity	Osteomalacia, osteoporosis; hyperparathyroidism; older age with history of falls or non-traumatic fractures; malabsorption; African-American or Hispanic ethnicity; medications affecting vitamin D*; chronic kidney disease; liver failure; pregnancy or lactation; obesity; granulomatous diseases; some lymphomas	Osteomalacia, osteoporosis; hyperparathyroidism; older age with history of falls or non-traumatic fracture; malabsorption; dark skin; medications affecting vitamin D*; chronic kidney disease; liver failure; pregnancy or lactation; obesity; granulomatous diseases
Retesting	No earlier than 3 months after commencing vitamin D supplements	No earlier than 3 months after commencing vitamin D supplements or change in dose No retesting required once target level reached (unless risk factors change)	After 3 months of vitamin D supplementation (high-risk individuals)		

* Glucocorticoids, azole antifungals, anticonvulsants or antiretroviral agents.

anticonvulsants or antiretroviral agents. For patients already taking vitamin D supplements, we also accepted testing for a new additional guideline-supported clinical indication, or documentation that the test was being performed to assess response to supplementation. Annual repeat screening of patients with CKD, with or without vitamin D therapy, was accepted given the progressive and dynamic nature of CKD-related mineral and bone disorder, although the disease-specific guidelines recommend treatment of VDD as for the general population.[11] Obesity was not included because recent data suggest that low serum 25OHD in obese individuals is more likely a consequence, rather than cause, of ill health.[12] We recorded non-guideline-supported indications where they were explicitly documented as the reason for testing.

The audit was performed in a tertiary referral hospital without maternity or paediatric services and involved detailed review of all serum 25OHD measurements (including local and regional requests) performed on adult inpatients and outpatients during a randomly selected one-week period from 1 December 2012 to 7 December 2012, inclusive.

We reviewed laboratory requests to identify the clinician's stated indication for measuring serum 25OHD and the patient's paper and electronic clinical records to identify other possible clinical indications for vitamin D testing, previous results and subsequent vitamin D-related follow-up management. Any guideline-supported indication identified in the clinical notes was accepted as the reason for 25OHD testing, even when this was not specifically documented as such. Where multiple reasons for testing were identified, the single most appropriate indication was recorded, with the most important regarded as being the treatment of osteoporotic fractures or falls, or the assessment of response to supplementation. Our interpretation of the indication for testing was purposely generous in order to limit the introduction of bias by the audit process itself.

An initial test was defined by the absence of serum 25OHD test results recorded in the previous 12 months. An initial test was considered to be consistent with guideline recommendations if there was a guideline-supported clinical indication or it was performed to assess response to supplementation for patients already on vitamin D and the test result was utilised appropriately. A repeat test was considered to be consistent with guideline recommendations if it was timed more than 90 days after the previous test, it was performed for a new guideline-supported indication or to assess response to vitamin D supplementation and the test result was utilised appropriately. Appropriate utilisation of test results included alteration or continuation of vitamin D supplementation in accordance with the result (e.g., increase in vitamin D dosage if serum 25OHD was low). Subsequent bone density measurement and laboratory investigations that would be reasonably expected to be performed to assess the cause or consequence of VDD (e.g., renal function, serum calcium, parathyroid hormone, coeliac serology) were also recorded.

During the audit period, serum 25OHD was measured routinely using the Architect 25OHD chemiluminescent microparticle immunoassay (Abbott Diagnostics, USA). Moderate/severe VDD (defined as 25OHD <30 nmol/L) or increased 25OHD (defined as >150 nmol/L) were verified by in-house liquid chromatography tandem mass spectrometry (LC-MSMS). The turnaround time for immunoassay results was typically less than 3 days but could take up to 7 days if LC-MSMS results were awaited. If LC-MSMS testing was awaited, an interim report was issued by the laboratory that was accessible electronically